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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,033	01/08/2008	Wei-Chiang Shen	89188.0151	5935

26021 7590 12/11/2009

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EXAMINER	
CHANDRA, GYAN	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
12/11/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/575,033	SHEN ET AL.	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *12-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/8/2007; 4/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Re: Shen et al
Date of priority: 10/10/2003

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-11) in the reply filed on 9/8/2009 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-30 are pending.

Claims 12-30 are withdrawn from further consideration as being drawn to nonelected inventions (i.e., groups 2-5).

Information Disclosure Statement

The Information Disclosure Statements (IDSs) filed on 11/08/2007 and 4/11/2008 have been considered.

Specification

Brief Description of the Figures

The Brief Description of the Figures is objected because Figure 8 comprises part (a) and (b). Therefore, to be consistent with the Figure legend, the Brief Description should be labeled as Figures 8 (a) and (b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 10, the phrase "Tf domain comprises at least one iron" and regarding claim 11, the phrase "the Tf domain comprises two iron molecules" render the claims indefinite because a Tf domain comprises amino acid sequence and not an iron molecule. The Tf domain can bind to at least one iron molecule or two iron molecules but the Tf domain does not comprise at least an iron molecule or two molecules. Therefore, the metes and bounds of the claims can not be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

For the purpose of comparing claims 11 and 12 with the prior art, it is noted that "Tf domain comprises (i) at least one iron molecule or (ii) two iron molecules" is interpreted as "Tf domain can bind to (i) at least one iron molecule or (ii) two iron molecules".

Claims 1-6 and 9-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Widera et al (previously presented, Pharmaceutical Res. 20: 1231-1238, 2003 (August)).

The instant claims are broadly drawn to a polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain, wherein the ability of the polypeptide to be transported into a cell expressing a transferring receptor (TfR) gene or the ability of the polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the G-CSF domain alone (claim 1), wherein the G-CSF domain and the Tf domain are linked through non-covalent bonding (claim 2), wherein the G-CSF domain and the Tf domain are linked through covalent bonding (claim 3), wherein the G-CSF domain and the Tf domain are linked through a disulfide bond (claim 4), wherein the polypeptide is a recombinant polypeptide (claim 5), wherein the G-CSF domain is linked to the Tf domain through a linker (claim 6), wherein the order of the G-CSF domain and the Tf domain is from the N-terminus to the C-terminus (Claim 9), and wherein Tf domain comprises two iron molecules (claims 10-11).

Widera et al teach a polypeptide conjugate comprising G-CSF and transferrin linked with a disulfide bond (page 1232, preparation of Tf-GCSF conjugate). They use a bifunctional cross-linking agent such as SPDP (n-succinimidyl 3-(2-pyridylthio) propionate to prepare said conjugate which introduces covalent linkage between G-CSF and Tf. It is noted that the polypeptide conjugate also comprises a number of ionic bonds between amino

acids of Tf and G-CSF. Therefore, meets the limitation of claim 2 which requires that Tf and G-CSF are linked through non-covalent bond. It is also noted that the polypeptide comprises G-CSF and Tf from the N-terminus to the c-terminus and therefore, meets the limitation of claim 9. The limitation of claim 5 is a product by process which does not carry a patentable weight. [W]hen the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. Additionally, it is well known in the art that a single chain transferrin polypeptide can bind two iron molecules (see Mouz et al., Nutrition 16: 229-230,2000). It is noted that the reference Mouz et al is applied to support the state of the art and not as a prior art. Therefore, the prior art of the record implicitly or explicitly anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widera et al in view of Friden et al (US Patent No. 5,672,683).

The instant claims are broadly drawn to a polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain, wherein the polypeptide is a recombinant polypeptide, and wherein said polypeptide is linked through a Leu-Glu linker.

The teachings of Widera et al are summarized as set forth supra. Widera et al do not teach expressing a fusion protein linked through Leu-Glu linker.

Friden et al teach making a fusion protein between transferrin and CNTF using a Leu-Glu linker (col. 23, Example 12). They teach expressing the fusion protein in host cell and teach that the fusion protein comprises the binding characteristics of transferrin as well as NGF. Therefore, transferrin would bind to iron two molecules.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to make fusion protein between G-CSF and transferrin as taught by Widera et al and include the Leu-Glu linker between G-CSF and Tf as taught by Friden et al. One of ordinary skill of the art would have been motivated to include the linker Leu-Glu between G-CSF and Tf because such a linker would provide more flexibility while retaining the characteristics of each protein as taught by Friden et al (Example 12). One would have a reasonable expectation of success in using Leu-Glu linker between G-CSF and Tf because Friden et al use this linker in a functionally equivalent fusion protein of CNTF and Trasferrin.

Claims 1, 3, 5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widera et al in view of Prior et al (US Patent No. 7,176,278).

The instant claims are broadly drawn to a polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain, wherein the ability of the polypeptide to be transported into a cell expressing a transferring receptor (TfR) gene or the ability of the polypeptide to be transported across a cell expressing a TfR gene via

transcytosis is higher than that of the G-CSF domain alone, wherein the G-CSF domain and the Tf domain are linked through covalent bonding, wherein the polypeptide is a recombinant polypeptide, and wherein the polypeptide of claim 5 further comprises a secretion signal at the N-terminus.

The teachings of Widera et al are summarized as set forth supra. Widera et al do not teach a fusion protein comprising a signal sequence at the N-terminus.

Prior et al teach making expression construct comprising a transcriptional promoter, a secretory signal sequence, a DNA sequence encoding a modified Tf fusion protein, wherein transferrin protein is joined to a DNA encoding a therapeutic protein of interest. Therefore, the Tf would be covalently joined with the protein of interest. They teach that any arrangement of the therapeutic protein or peptide fused to or within the Tf portion may be used in the vectors of the invention. They teach that the selection of suitable promoters, signal sequences and terminators will be determined by the selected host cell and will be evident to one skilled in the art (col. 47, Vectors). Prior et al teach making fusion proteins such as EMP1/Tf (col. 67, Example 2), GLP-1-Tf (col. 71, Example 3), beta IFN/Tf (col. 73, example 4), soluble Toxin receptor/Tf (col. 76, Example 5).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to make fusion protein between G-CSF and transferrin as taught by Widera et al and include a signal sequence as taught by Prior et al. One of ordinary skill of the art would have been motivated to include a signal sequence to the N-terminus of G-CSF and Tf fusion polypeptide because signal sequences

are used as a leader sequence for exporting protein out of the cell expressing the protein of interest as taught by Prior et al (col. 47, Vectors). One would have a reasonable expectation of success in using a linker sequence suitable for expressing a polypeptide fusion between G-CSF and Tf because Prior et al teach selecting a signal sequence suitable for expressing a protein in a host cell.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

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9199 (IN USA OR CANADA) or 571-272-1000.

/Gyan Chandra/
Examiner, Art Unit 1646